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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

Office Action Summary	Application No.	Applicant(s)	
	10/801,342	HWANG ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007 and 19 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *1-7,15,17,18 and 33-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14,16 and 19-32* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/07*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claim Status

1. Applicant's amendments submitted on February 2, 2007 and March 19, 2007 are acknowledged. Applicant has withdrawn claims 1-7, 15, 17-18; amended claims 8-10, 12, 14 and added new claims 21-65.

2. Newly submitted claims 33-65 are directed to multiple inventions that are independent or distinct from the invention originally claimed for the following reasons: The newly submitted claims are apparatus claims directed to different shapes and characteristics of the reaction vessel, such as channels that are used in microchips that are different from the originally claimed apparatus where only a generic reaction vessel was claimed. The limitations associated with the various permutations of shapes/characteristics of the reaction vessels along with the arrangements of heating elements will result in different structural requirements thereby resulting in many independent /distinct instruments and have been claimed as such.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 33-65 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Currently claims 1-65 are pending in the application. Newly added claims 21-32 depend from amended claim 8 and will be examined with other claims that

depend from claim 8. Claims 8-14, 16, 19-32 are being examined in this Office Action.

Specification

4. Applicant's remarks and evidence provided in the paper filed on March 19, 2007 regarding the amendment filed on August 23, 2006 have been fully considered and are found persuasive. Accordingly the new matter objection to specification is withdrawn and Replacement paragraph [0064] is entered.

Priority

5. The current US application was filed on March 15, 2004 as a CIP of PCT/KR02/01728 application filed on September 14, 2002. For claims that find support in the PCT application priority of September 14, 2002 is being given , while for claims that were added on to PCT in the present CIP, the priority of March 15, 2004 is being granted. Applicant does not get benefit of earlier Korean (foreign) applications filed on September 15, 2001 and October 30, 2001 respectively.

Claim Objections

6. Amendments to claims 9-10 and 12 obviate the issues raised regarding these claims in previous Office Action. Accordingly the objections to these claims are withdrawn.

7. Newly added claim 27 is objected to because of the following informalities: The claim is lacking a period at the end. Appropriate correction is required.

<u>Response to arguments re 103 rejections of claims 8-9 and 19-20 over Hunicke-Smith in view of Benett et al.</u>

8. Applicant's arguments filed on March 19, 2007 have been fully considered but they are not persuasive.

At the outset Applicant argues that Benett et al. does specifically teach upper temperature zone located lower in height than a relatively low temperature zone. Examiner would like to point out that Fig. 1 shows upper temperature zone. It is marked by number 13 and is located lower in height than a relatively low temperature zone marked by number 14 in the figure. Also see page 5, lines 20-23 where "Upper Temperature Zone 13" and "Lower Temperature Zone 14" are explicitly taught.

Applicant further argues that in the Figure 1 Upper Temperature Zone 13 is shown to partially overlap with the Lower Temperature Zone 14 and therefore no prima facie case of obviousness has been made by the office. Examiner would like to point out that there is no limitation in the claims that the zones do not overlap.

Applicant further argues that references cited do not teach a 'straight cylinder or tube' . Hunicke-Smith actually uses capillary as reaction vessels and thus indeed does teach 'straight cylinder or tube' (see Hunicke Smith page 2 line 9, where capillary tube is taught).

Applicant argues that Benett et al. teaches high and low temperature regions in one of the two vertical channels and the lower temperature zone in another of vertical channels. Examiner would like to point out that a careful reading of Benett et al. (see page 6 lines 3-8) will indicate to Applicant that the PCR system shown in Fig. 1 is constructed using two chamber halves 16 and 17.

So its entirely feasible that heater for zone 13 is located on one half and the heater for zone 14 is located in the other half. The reference is silent about which half the heaters are located on. Irrespective of which half the two heaters were located, when the two halves are assembled to form the reaction chamber then tops part of both the channels (12 a and 12 b) is subjected to lower temperature and bottom part of both the channels (12 a and 12 b) is subjected to higher temperature.

Examiner would like to point out that Applicant has erroneously concluded that Benett et al. teach unidirectional flow. Benett et al. teach convection flow of fluid generated by having a higher temperature at bottom and lower temperature at upper end. This flow is inherently bidirectional. As molecules get heated they rise and cooler molecules come down to replace them this sets up the convention current. So by definition in convention some molecules are going up while others come down hence the flow is bidirectional. Again for pictorial depiction purposes since low temp zone 14 is marked on right side of Fig. 1, the arrows are shown to come down on that side. While the high temp zone is marked on the left side of Fig. 1, the arrows are shown to come up on that side.

It should be noticed that Benett et al teach heating **specific section** of the channel namely top section or bottom section (It should be noted that Benett et al. do not teach heating specific channels i.e. subjecting channel 12a to high temp while subjecting channel 12c to lower temperature).

Hunicke-Smith does teach a reaction vessel with a single straight cylinder or tube and one that has two ends.

Therefore all elements of claim 8 are taught to one of ordinary skill at the time of invention in view of teaching of Hunicke-Smith and Benett et al. Therefore the invention was obvious to one of ordinary skill at the time the invention was made. Hence Examiner is maintaining the rejection of claims 8-9 and 19-20 over Hunicke-Smith and Benett et al.

All the other remaining claims were rejected over some supporting reference in view of Hunicke-Smith and Benett et al. Since Hunicke-Smith and Benett et al. properly renders claim 8 obvious. All other claims that depend from claim 8 and were rejected over other secondary references they are being maintained all the other rejections of claims previously presented, all those rejections are being maintained as well.

Double Patenting Rejection

9. Applicant has not addressed the double patenting rejection that was made in the previous office action and thus it is also being maintained.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 8-9 and 19-22, 25-27 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunicke-Smith WO 97/48818 published 24 December 1997 (cited by applicant in the IDS) in view of Benett et. al. WO 02/072267 A1 filed 22 February 2002 with US priority date of 9 March 2001 (cited by applicant in the IDS).

A) Regarding claim 8, Hunicke-Smith teaches :

A nucleic acid sequence amplification apparatus using PCR (see page 2, lines 5-6 where Hunicke-Smith teaches an apparatus for thermally cycling a DNA sample (another name used in the art for PCR is taught),

which apparatus comprises: a plurality of heat sources (see page 2, lines 6-7 where Hunicke-Smith teaches first and second heating elements)

which may supply heat to (see page 2, lines 7-12, where Hunicke-Smith teaches the heating chambers that contact the capillary tube containing sample),

or remove heat from (see page 3, lines 6-7, where Hunicke-Smith teaches a heating unit assembly further containing a cooling element that can remove heat from *sample contained in reaction vessel* (capillary in this case)).

Wherein the reaction vessel is configured as a straight cylinder or tube. (Hunicke-Smith teaches capillary as a reaction vessel. By teaching capillary Hunicke-Smith teaches the shape of reaction vessel as a straight cylinder or tube (see page 2 line 9, where capillary tube is taught as a reaction vessel)

Hunicke-Smith teaches selected first and second elevated temperature (page 2, lines 11-12).

Hunicke-Smith teaches "*wherein the specific temperature distribution fulfilling a temperature condition suitable for (i) a denaturation step in which double strand DNAs become separated to single strand DNAs,* (see page 2, lines 14-15, where Hunicke-Smith teaches temperature that is effective to denature the DNA sample) *(ii) an annealing step in which the single strand DNAs formed in the denaturation step hybridize to the primers to form DNA-primer complexes, or (iii) a polymerization step in which the primers in the DNA-primer complexes are extended by the polymerization reaction* (see page 2, lines 15-16, where Hunicke-Smith teaches second temperature at which DNA annealing and primer directed DNA polymerization can occur).

Regarding claim 19, Hunicke-Smith teaches: *wherein the plurality of heat sources* (see page 2 lines 7-9, where first and second heating elements defining first and second heating chambers are taught) *comprises a first thermally conductive solid that is in contact with a lower portion of the reaction vessel and*

a second thermally conductive solid that is in contact with an upper portion of the reaction vessel.(see Fig. 1A and page 7, lines 27-32 where heating unit assemblies are taught. Each heating unit assembly contains at least two heating elements, such as first heating element 24 that is in contact with a lower portion of reaction vessel (capillary) and a second heating element 26 that is in contact with an upper portion of the reaction vessel (capillary). The desired temperature in these heating elements is maintained by utilizing independently controlled heating elements, such as elements 24 and 26 using power transistors in integrated chips and microprocessors (see page 8, lines 13-24). It is well known in the art that transistors and microprocessors on integrated chips are solids and the fact elements 24 and 26 serve as heating elements indicates they are de facto conductive solids. Thus Hunicke-Smith teaches thermally conductive solids.

Regarding claim 20, Hunicke-Smith teaches: *The nucleic acid sequence amplification apparatus of claim 19, wherein the plurality of the heat sources further comprises a third thermally conductive solid that is in thermal contact with an intermediate portion of the reaction vessel in between the upper and lower portion.* (see page 14, lines 4-10, where 3 separate heating chambers, formed by 3 separate heating elements and preferably containing 3 separate temperature sensors-one for each heating element are taught. They teach that the third chamber of each assembly provides a third temperature zone though which the DNA sample may be cycled thus accomplishing 3 temperature PCR employing a denaturing temperature (high temperature), an annealing temperature (low temperature) and an extension (intermediate temperature). It should be noted

that Hunicke-Smith does not explicitly state that the third thermally conductive solid is in thermal contact with an intermediate portion of the reaction vessel in between the upper and lower portion. Fig. 5 shows 3 heating elements 110, 112, 114. But no reference is made about spatial temperature distribution ie. intermediate temperature is the portion between the upper and lower portion.

Regarding claim 21, *Hunicke-Smith teaches: wherein the reaction vessel is vertical with respect to the heat sources. (see Fig.* 5 where heating elements 110, 112 are shown as two heating sources. These two are shown arranged horizontally and the capillary tubes (reaction vessel) are vertical with respect to the heat sources.

Regarding claim 25, *Hunicke-Smith teaches:* wherein the reaction vessel is pressurized. (see page 9, lines 28-31 where air pressure generated in the reaction vessel by mechanical element syringe is taught. Thus *Hunicke-Smith* teaches wherein the reaction vessel is pressurized)

Regarding claim 27, *Hunicke-Smith teaches:* wherein the reaction vessel comprises a top end and a bottom end. (see page 9, lines 3-8 where capillary with top end and bottom end is described as a reaction vessel).

Regarding claim 32, *Hunicke-Smith teaches:* wherein the apparatus further comprises multiple reaction vessels (see Fig. 1A).

B) Regarding claim 8 Hunicke-Smith does not teach spatial temperature distribution therefore following elements related to spatial temperature distribution in the claim are not taught by Hunicke-Smith: *a plurality of specific regions in a sample contained in a reaction vessel, wherein the heat sources are*

arranged to maintain a specific spatial temperature distribution in the sample such that a relatively high temperature region is located lower in height than a relatively low temperature region.

, and wherein the specific spatial temperature distribution is a temperature distribution that induces circulation of the sample by thermal convection so that the denaturation, annealing, and polymerization steps occur sequentially and repeatedly inside the sample".

C) Regarding claim 8, Benett et al. teach:

a plurality of specific regions in a sample contained in a reaction vessel (see Fig. 3 where Benett et al. teach two sample regions marked 13 and 14 in a reaction vessel), *wherein the heat sources are arranged to maintain a specific spatial temperature distribution in the sample such that a relatively high temperature region is located lower in height than a relatively low temperature region* (see page 5, lines 20-23 where Benett et al. teach a relatively high temperature region called the "Upper Temperature Zone 13" located lower in height than a relatively low temperature region called "Lower Temperature Zone 14". Bennett et al. teach that by heating specific sections a convection cell is created thereby necessarily teaching that the heat sources are arranged to maintain a specific spatial temperature distribution in the sample such that a relatively high temperature region Zone 13 is located lower in height than a relatively low temperature region Zone 14.

In view of above teaching it is necessary that the intermediate temperature zone required for PCR extension will be a located in between the upper low

temperature zone 14 and lower high temperature zone 13. Therefore clear description of spatial localization of high temperature zone to bottom and low temperature zone to top provides support to the conclusion that the intermediate temperature zone and the third heating element recited in claim 20 and taught by Hunicke –Smith is actually located in a region in between the upper and lower portion.

Regarding claim 9, Benett et al. teach *wherein at least one of the heat sources comprises a thermally conductive solid in thermal contact with a specific region of the reaction vessel or the sample* (see page 5 line 23 where Benett et. al teach thermally conductive solid such as platinum heater as a heat source that is in contact with zone 13 of the reaction vessel; also see page 8, lines 11-14).

Regarding claim 22, Benett et al. teach *wherein the thermal convection is bidirectional.* (see Fig. 1. where bidirectional convention is shown flow of liquid is going one direction in channel 12a and flow of liquid in channel 12c is going in the other direction. Thus, Benett et al. teach *wherein the thermal convection is bidirectional.*

Regarding claim 26, Hunicke Smith and Benett et al. teach the apparatus of claim 8. The limitation wherein "the spatial temperature distribution of the reaction vessel further comprises a convention region positioned between the relatively high temperature region and the relatively low temperature region" does not provide any further structural limitation to the apparatus of claim 8 since the limitation addresses a phenomenon that occurs in the sample when placed in the apparatus. Hence this claim is not being further examined.

It would have been *prima facie* obvious to one of ordinary skill in the art to combine the structural elements taught by Benett et al. in the PCR apparatus taught by Hunicke-Smith. The motivation to do so is provided by Benett et. al. who teach the inefficiency associated with the conventional PCR machines where heating and cooling of material other than the PCR sample itself. They state "There is an increasing need to build smaller more portable PCR systems for use in the field and clinical settings.----This embodiment of the present invention provides a convectively driven PCR thermal-cycling system 10" (see Benett et. al. page 5, lines 7-14). Thus by combining the structural elements taught by Hunicke –Smith with the elements taught by Benett et. al. one would get a more efficient PCR apparatus that is capable of convective circulation thereby eliminating the cumbersome and contamination prone plunger system of moving the samples of Hunicke-Smith within the reaction vessel. Further Benett et al. point out that their system is also amenable to miniaturization as is intended by the applicant.

13. Claims 10-12, 14 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunicke-Smith and Benett et al. as applied to claim 8 above, and further in view of Haff et al. US.Pat. 5,720,923 issued February 24, 1998.

Regarding claims 9-12, Hunicke-Smith and Benett et. al. teach the PCR apparatus of claim 8 but do not specifically teach thermally conductive solid, liquid or gas as heat sources.

Regarding claim 9, Haff et al. teach *at least one of the heat sources comprises a thermally conductive solid in thermal contact with a specific region of*

the reaction vessel or the sample; and a heating unit that supplies heat to the thermally conductive solid (see col. 3, lines 66-67 and col 4, lines 1-3 where Haff et. al. teach two metal blocks each of which has its temperature stabilized at one of two temperatures (denaturation and anneal/extend incubation) needed for PCR that are in thermal contact with the sample in the reaction vessel (capillary tube)). Thus Haff et al. teach heat sources that are thermally conductive solid (metal blocks) in thermal contact with reaction vessel. By teaching blocks stabilized at temperatures required for PCR, a heating unit that supplies heat to these metal blocks is taught by Haff et. al.

Regarding claims 10-11, Haff et al. teach *wherein at least one of the heat source comprises a liquid in thermal contact with a specific region of the reaction vessel; a receptor in which the liquid is to be contained; and a heating unit that supplies heat to the liquid and wherein at least one of the heat sources further comprises a circulation unit that circulates the liquid around the reaction vessel.* (see col. 3, lines 45-54 where Haff et al. teach use of two or three temperature stable fluid baths, each of which is constantly circulating its fluid through a separate conduit. Each fluid bath is thermostatted at one of the necessary PCR incubation temperatures (this teaching implies that the liquid in the bath is being heated by a heating unit and perhaps there is also a cooling unit that is helping to maintain the temperature required by the thermostat) this liquid of the fluid bath is in thermal contact with capillary (reaction vessel) containing the reaction mixture.)

Regarding claim 12, Haff et al. teach *at least one of the heat sources comprises a gas in thermal contact with the reaction vessel; a heating unit that supplies heat to the gas and a circulation unit that circulates the gas around the reaction vessel.* (see col. 2, lines 10-19, where an oven with a heating coil (source of heat), a solenoid activated door and a fan (to circulate gas) are taught. Here Air was used as the heat transfer medium. The samples in capillary tubes are placed in this oven). Thus Haff et al. teach gas in thermal contact with the reaction vessel; a heating unit that supplies heat to the gas and a circulation unit that circulates the gas around the reaction vessel.

Regarding claim 14, Haff et al. teach *which apparatus comprises a means for insulating heat transfer between the heating sources.*(see col. 7, lines 30-33 and Fig.1 where high temperature bath 16 and low temperature bath 18 are separated by a layer of insulation 20 which is selected to minimize the flow of heat between the two baths 16 and 18. Also see col. 15, lines 54-58 where layer of insulation 174 separating metal block heat exchangers 170 and 72 are taught).

Regarding claim 23, Haff et al. teach wherein the insulating means is a solid, liquid or a gas. (see col. 15, lines 54-58 where layer of insulation 174 separating metal block heat exchangers 170 and 72 are taught)

It would be *prima facie* obvious to one of ordinary skill in the art to combine the structural elements of the PCR apparatus taught by Haff et al. in the PCR apparatus taught by Hunicke-Smith and Benett et. al. The motivation to do so is provided by Haff et. al. because not only does Haff et. al. teach solid, liquid and gas sources of heat each of them having their own advantages as system of

heat transfer but they also teach use of insulation between different heat sources as a means of insulating heat transfer between heating sources. In addition they teach use of Peltier device to control temperature of the metal blocks (see col. 16, lines 12-14). Thereby allowing each heat source to efficiently maintain the desired temperature.

14. Claims 24 and 28-30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hunicke-Smith; Benett et al. and Haff et al. as applied to claims 8, 23 and 27 above further in view of Bedingham et al. (U S Pat. 6,734,401 B2 filed on June 28, 2001).

Regarding claim 24, Hunicke-Smith; Benett et al. and Haff et al. teach the apparatus of claim 23, wherein insulating means is solid, liquid or a gas. Haff et al. teach an insulating means but do not explicitly recite whether the insulating means is a solid, liquid or gas.

Regarding claim 24, Bedingham et al. teach wherein the insulating means is air (see col. 39 line 35 and line 60-61 where air is taught as insulating material)

Regarding claim 28, Bedingham et al. teach wherein the reaction vessel is tapered. (See col. 32, lines 56-61 where tapered reaction vessel 844' is taught)

Regarding claim 29, Bedingham et al. teach wherein the reaction vessel is tapered from the top end to the bottom end. (See col. 32, lines 56-61 where tapered reaction vessel 844' is shown tapered from the top end to the bottom end).

Regarding claim 30, Bedingham et al. teach wherein the reaction vessel is tapered from the bottom end to the top end (see Fig. 24B where reaction vessel tapered from the bottom end to the top end is shown)

It would have been prima facie obvious to one of ordinary skill in the art to combine the use of air as insulating means taught by Bedingham et al. in the PCR apparatus taught by Hunicke-Smith; Benett et al. and Haff et al. The motivation to do so is provided by Bedingham et al. who teach a device for thermal cycling that is useful for processing multiple samples simultaneously. The device uses electromagnetic energy to heat the base. Both the base plate and the device are rotated around an axis of rotation. In such a device air is used as insulating mean. Bedingham et al. state "Thermal isolation of a process chamber 1650 in the device can be enhanced by removing material around the process chamber 1650-------. Essentially, the process chamber 1650 is surrounded by one or more voids. Channels to deliver-----. Thermal isolation is improved by removing material around the ring 1652 that could serve as a heat sink, drawing thermal energy away from the process chamber 1650 during heating, or supplying stored thermal energy to the process chamber when cooling is desired" (see Bedingham et al. col. 39, lines 17-31).

15. Claims 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hunicke-Smith and Benett et. al. as applied to claim 8 above, and further in view of Northup WO 98/25701 published 18 June 1998 (cited by applicant in the IDS).

Regarding claim 13 Hunicke-Smith and Benett et. al. teach the PCR apparatus of claim 8 but do not teach wherein at least one of the heat sources is an infrared radiation generating unit that supplies heat directly to the sample.

Regarding claims 13, Northup teaches *wherein at least one of the heat sources is an infrared radiation generating unit that supplies heat directly to the sample* (see page 12, last 3 lines in bottom of page, where Northup teaches use of Infra Red (IR) source and Fig.3. where IR source 17 applies heat to solution in chamber 31.

It would be *prima facie* obvious to one of ordinary skill in the art to combine the structural elements of the PCR apparatus taught by Northup in the PCR apparatus taught by Hunicke-Smith and Benett et. al. The motivation to do so is provided by Northup who teach advantages associated with integrated microfabricated reactor developed for in situ chemical reactions, which is especially advantageous for biochemical reactions which require high precision thermal cycling, particularly DNA-base manipulations such as PCR, since small dimensions of microinstrumentation promote rapid cycling times (see page 4, par. 1).

16. Claims 16 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunicke-Smith and Benett et al. as applied to claims Claims 8 and 27 above, and further in view of Macho et. al. US Pat. No. 5,919,622 issued July 6, 1999 (cited by applicant in the IDS).

Regarding claim 16, Hunicke-Smith and Benett et. al. teach the PCR apparatus of claim 8 but do not teach wherein heat source is shaped to comprise

at least one protrusion that fits in an opening of the reaction vessel, wherein said protrusion contacts the sample.

Regarding claim 16, Macho et. al. teaches *wherein the heat source is shaped to comprise at least one protrusion that fits in an opening of the reaction vessel, wherein said protrusion contacts the sample* (see col. 5, lines 14-25 where Macho et. al. teach a heat source that dips into the vessel in a manner that the liquid receives an adequate amount of heat. Also see Fig 1. where protrusion 5 is shown to fit in an opening of the reaction vessel through stopper 3 with a lid 1 attached to it).

Regarding claim 31, Macho et al. teach use of reaction vessel wherein the bottom end is closed for PCR. They teach use of PCR in vessel that has (See Fig. 1 and 2 and col. 2, lines 25-28). The PCR vessels shown have bottom end closed and an open top end that can be closed by using a lid.

It would be *prima facie* obvious to one of ordinary skill in the art to combine the structural elements of the PCR apparatus taught by Macho et. al. in the PCR apparatus taught by Hunicke-Smith and Benett et. al. The motivation to do so is provided by Macho et. al. who state "The subject of the invention is a system for the temperature adjustment treatment of nucleic acid containing liquids in a vessel which has a reusable thermostat element and a disposable heating element, whereby heating element is a integral part of the vessel or the vessel lid and is dipped into the liquid during the treatment" see col. 2. lines 12-17. Also see col. 10 lines 63-64 where Macho et. al. teach a heating element where the resistance wire extended about two thirds of the way into the PCR mix.

Besides providing a source of heat, such a disposable arrangement also provides a means to selectively introduce a component such as polymerase into the reaction to start the reaction.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 8, 16 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7 and 8 of copending Application No. 10/836,376. Although the conflicting claims are not identical, they are not patentably distinct from each other because the PCR apparatus described in claims 7 and 8 of copending application make the PCR apparatus claimed in claims 8, 16 and 20 of the instant application obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. All claims under consideration 8-14, 16 and 19-32 are rejected over prior art.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

Teresa Strzelecka
TERESA E. STRZELECKA, PH.D.
PRIMARY EXAMINER
5/29/07